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EXAMINER	
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ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
04/22/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/566,100	TORRENS JOVER ET AL.	
	Examiner	Art Unit	
	UMAMAHESWARI RAMACHANDRAN	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *6-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 30-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/27/2006, 4/18/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election of the following species in the reply filed on 2/4/2010 is acknowledged. Applicants have provisionally elected the following species: (1) 2-(4-(8-methyl-2-oxo-2,4-dihydro- 1H-benzo [d] [1,3]oxazin- 1 -yl)piperidin- 1 -yl)-N-(9- oxo-9H-fluoren-3-yl)acetamide hydrochloride as a compound binding NPY5 receptor (at least claims 1 - 41 readable thereon) (2) N-[3-(2-dimethylaminoethyl)-1H-indol-5-yl]-5-chloronaphthalene-2-sulphonamide as a compound binding 5-HT6 receptor (at least claims 1 - 41 readable thereon) (3) regulation of appetite as the disease.

Applicants' argue that the Office has not provided any reasons or examples to support a conclusion that the species are indeed patentably distinct and submit that the restriction is improper. In response, applicants claim an active substance combination comprising at least one compound with neuropeptide Y (NPY) receptor affinity of formula I a , and at least one compound with 5-HT6 receptor affinity of formula I b. Compounds of formula I(a) can be structurally different. For example when R10a and R11a together with the bridging nitrogen atom form an optionally at least mono-substituted, saturated, unsaturated or aromatic heterocyclic ring that may contain at least one further heteroatom as a ring member and/or may be condensed with an optionally at least mono-substituted mono- or polycyclic ring system that is structurally distinct from a compound where R10a = R11a = H, which is amide compound. If the substitutions on the 1, 4 disubstituted piperidine compounds of formula I(a) is for example, heteroaryl aryl radical the derivatives are structurally distinct based on the heteroatoms(O, N, S, P etc) and based on the ring system (3 or 4 or 5 or 6 or 7

membered ring). Also, applicants' claim the use of combination of compounds with neuropeptide Y (NPY) receptor affinity and compounds with 5-HT6 receptor affinity for treating a variety of diseases as listed above. Each disease has a different and distinct etiology and pathophysiological manifestations, and that each is differently treated. Such is sufficient to indicate that each of the methods of treating the presently claimed disease states is differently searched in the patent and non-patent literature and that a search for one disease will not necessarily result in a comprehensive search of any one or more of the diseases listed. As a result, an undue burden would be placed on the Examiner to search each of Applicant's presently claimed species. Hence the requirement for restriction/election is deemed proper and is made Final.

Claims 6-29 do not read on the elected species for disease – regulation of appetite. Hence they are withdrawn from consideration. Claims 1-5, 30-41 read on the elected species and will be examined on the merits herein.

Application Priority

This application is a 371 of PCT/EP04/08515, 07/29/2004 and claims priority from foreign application, SPAIN P200301814, 7/30/2003.

Information Disclosure Statement

The information disclosure statements (IDS) filed on 1/27/2006 and 4/18/2006 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the IDS is being considered by the Examiner.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5, 30-41 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 4-9, 34-45 of copending Application No. 10/566,402. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant application and the co-pending application teaches an active substance combination of at least one compound with neuropeptide receptor NPY affinity of formula I a with at least one compound with 5-HT6 receptor affinity of formula I b and further claims the use of such compounds in treating various disorders including regulation of appetite (elected species).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 3, 4 and 30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22, 29 of copending Application No. 10/565,979 in view of Jover et al. (US 2004/0058920, filing date Apr 4 2003) and further in view of Merce-Vidal et al. (U.S. 7,105,515, effective filing date Nov 13 2002) and Caldirola et al. (U.S. 7,144,883, effective filing date, June 11 2002).

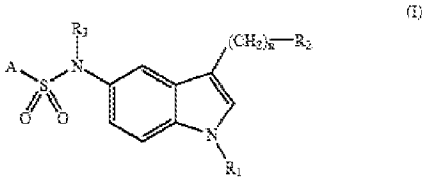
Claims 1, 3, 4 and 30 are towards the pharmaceutical composition or medicament of the compounds comprising 1,4 disubstituted piperidines of compounds of formula I a and at least one compound with 5-HT6 receptor affinity of formula I b.

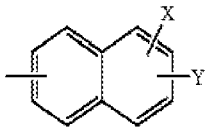
The claims of the co-pending application '979 towards the pharmaceutical composition or medicament of the compounds comprising 1,4 disubstituted piperidines compounds as instantly claimed.

The co-pending application does not teach an active substance combination with at least one additional compound with 5-HT6 receptor affinity of formula I b.

Jover et al. teaches benzoxazinone- derived compounds of formula I as claimed in the instant application as well of the co-pending application, their compositions and their use as a medicament in treatment of humans or animals (see abstract, para 0010). The reference teaches the compounds as neuropeptide Y receptor regulators are useful for the regulation of food ingestion (para 009) and in the treatment of treatment of disorders of food ingestion, preferably obesity, anorexia or bulimia (para 0285).

The reference Merce-Vidal teaches derivatives of sulphonamides (see abstract).



When R1=H, n=0, A=  , R3=H the reference teaches the elected species for 5-HT6 (see col. 2, lines 50, 65, 67, col. 3, line 24). Merce-Vidal teaches that the compounds have 5-HT6 serotonin receptor antagonistic activity useful in the preparation of medicament for prevention or treatment of various CNS (central nervous system) disorders.

Caldirola et al. teaches substituted sulfonamide compounds with 5-HT6 receptor affinity to be useful for the prophylaxis and treatment of medical conditions relating to obesity, type II diabetes and/or disorders of the central nervous system (see abstract, col. 2, lines 31-35).

It would have been obvious to one having ordinary skill in the art at the time of the invention to have combined a 1,4 disubstituted piperidine compounds of the co-pending application with that of a compound with 5-HT6 serotonin receptor affinity from the teachings of Jover and Merce-Vidal. Jover teaches that 1,4 disubstituted piperidine compounds of the co-pending application has neuropeptide Y (NPY) affinity and the compounds can be used in treating obesity disorders and Merce-Vidal and Caldirola teaches the use of 5-HT6 receptor binding compounds to be useful in obesity, CNS disorders. It would have been obvious to one having ordinary skill in the art at the time

of the invention to have made a combination or a formulation or a medicament of at least one compound of the 1,4 disubstituted piperidine compounds claimed with at least one compound with 5-HT6 receptor affinity because both of them have been taught in the prior art to be useful in a method of treating obesity disorders.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 3, 4 and 30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 19-23 of copending Application No. 10/566,399 in view of Merce-Vidal et al. (U.S. 7,105,515) and Caldirola et al. (U.S. 7,144,883).

Claims 1, 3, 4 and 30 are towards the pharmaceutical composition or medicament of the compounds comprising 1,4 disubstituted piperidines of compounds of formula I a and at least one compound with 5-HT6 receptor affinity of formula I b.

The claims of the co-pending application '399 are towards the pharmaceutical composition or medicament of some of the compounds comprising 1,4 disubstituted piperidines compounds as instantly claimed and the use of such compositions in regulation of appetite, obesity, CNS disorders etc.

Merce-Vidal and Caldirola et al. teachings discussed as above.

It would have been obvious to one having ordinary skill in the art at the time of the invention to have combined a 1, 4 disubstituted piperidine compounds of the co-pending application with that of a compound with 5-HT6 serotonin receptor affinity from the teachings of Merce-Vida and Caldirola. Merce-Vidal and Caldirola teaches the use

of 5-HT6 receptor binding compounds to be useful in obesity, CNS disorders. It would have been obvious to one having ordinary skill in the art at the time of the invention to have made a combination or a formulation or a medicament of at least one compound of the 1, 4 disubstituted piperidine compounds claimed with at least one compound with 5-HT6 receptor affinity because both of them have been taught in the prior art to be useful in a method of treating CNS, obesity disorders etc

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 3-5 and 30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 18 of U.S Patent No. 7,056,914 in view of Jover et al. (US 2004/0058920) and further in view of Merce-Vidal et al. (U.S. 7,105,515) and Caldirola et al. (U.S. 7,144,883).

Claims 1, 3-5 and 30 are towards the pharmaceutical composition or medicament of the compounds comprising 1,4 disubstituted piperidines of compounds of formula I a and at least one compound with 5-HT6 receptor affinity of formula I b and the use of such compositions in various disorders including regulation of appetite, CNS disorders etc.

The claims of the patent are towards the pharmaceutical composition or medicament of the compounds comprising 1, 4 disubstituted piperidines compounds as instantly claimed.

The co-pending application does not teach an active substance combination with at least one additional compound with 5-HT6 receptor affinity of formula I b.

Jover et al, Merce-Vidal and Caldirola et al. teachings discussed as above.

It would have been obvious to one having ordinary skill in the art at the time of the invention to have combined a 1, 4 disubstituted piperidine compounds of the co-pending application with that of a compound with 5-HT6 serotonin receptor affinity from the teachings of Jover and Merce-Vidal. Jover teaches that 1,4 disubstituted piperidine compounds of the co-pending application has neuropeptide Y (NPY) affinity and the compounds can be used in treating obesity disorders and Merce-Vidal and Caldirola teaches the use of 5-HT6 receptor binding compounds to be useful in obesity, CNS disorders. It would have been obvious to one having ordinary skill in the art at the time of the invention to have made a combination or a formulation or a medicament of at least one compound of the 1, 4 disubstituted piperidine compounds claimed with at least one compound with 5-HT6 receptor affinity because both of them have been taught in the prior art to be useful in a method of treating obesity disorders.

Claims 1, 3-5 and 30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3 of U.S Patent No. 7,041,665 in view of Jover et al. (US 2004/0058920) and further in view of Merce-Vidal et al. (U.S. 7,105,515) and Caldirola et al. (U.S. 7,144,883).

Claims 1, 3-5 and 30 are towards the pharmaceutical composition or medicament of the compounds comprising 1,4 disubstituted piperidines of compounds of formula I a and at least one compound with 5-HT6 receptor affinity of formula I b and the use of such compositions in various disorders including regulation of appetite, CNS disorders etc.

The claims of the patent are towards the pharmaceutical composition of the compounds comprising 1, 4 disubstituted piperidines compounds as instantly claimed.

The co-pending application does not teach an active substance combination with at least one additional compound with 5-HT6 receptor affinity of formula I b.

Jover et al, Merce-Vidal and Caldirola et al. teachings discussed as above.

It would have been obvious to one having ordinary skill in the art at the time of the invention to have combined a 1,4 disubstituted piperidine compounds of the co-pending application with that of a compound with 5-HT6 serotonin receptor affinity from the teachings of Jover and Merce-Vidal. Jover teaches that 1,4 disubstituted piperidine compounds of the co-pending application has neuropeptide Y (NPY) affinity and the compounds can be used in treating obesity disorders and Merce-Vidal and Caldirola teaches the use of 5-HT6 receptor binding compounds to be useful in obesity, CNS disorders. It would have been obvious to one having ordinary skill in the art at the time of the invention to have made a combination or a formulation or a medicament of at least one compound of the 1,4 disubstituted piperidine compounds claimed with at least one compound with 5-HT6 receptor affinity because both of them have been taught in the prior art to be useful in a method of treating obesity disorders.

Claims 1, 3-4 and 30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 of U.S Patent No. 7,514,429 in view of Merce-Vidal et al. (U.S. 7,105,515) and Caldirola et al. (U.S. 7,144,883).

Claims 1, 3-4 and 30 are towards the pharmaceutical composition or medicament of the compounds comprising 1, 4 disubstituted piperidines of compounds of formula I a and at least one compound with 5-HT6 receptor affinity of formula I b and the use of such compositions in various disorders including regulation of appetite, CNS disorders, pain, depression, epilepsy, anxiety, depression, hypertensive syndrome disorder, diabetes, food digestion disorders etc

The claims of the patent are towards the method of use of the compounds comprising 1,4 disubstituted piperidines compounds as instantly claimed and the use is towards treating food digestion disorders, obesity, bulimia, pain, depression, anxiety, hypertensive syndrome, diabetes etc

The co-pending application does not teach an active substance combination with at least one additional compound with 5-HT6 receptor affinity of formula I b.

Merce-Vidal and Caldirola et al. teachings discussed as above.

It would have been obvious to one having ordinary skill in the art at the time of the invention to have combined a 1, 4 disubstituted piperidine compounds of the co-pending application with that of a compound with 5-HT6 serotonin receptor affinity from the teachings of Merce-Vidal. Merce-Vidal and Caldirola teaches the use of 5-HT6 receptor binding compounds to be useful in obesity, CNS disorders. It would have been obvious to one having ordinary skill in the art at the time of the invention to have made a combination or a formulation or a medicament of at least one compound of the 1, 4 disubstituted piperidine compounds claimed with at least one compound with 5-HT6

receptor affinity because both of them have been taught in the prior art to be useful in a method of treating obesity disorders.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 30-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification while providing guidance of how to make the compounds or prima facie modification of such compounds to its pharmaceutically addition salt with pharmaceutically acceptable acids, does not provide enablement for making unknown solvates. The specification does not enable any person skilled in the art of synthetic organic chemistry to make the invention commensurate in scope with these claims. "The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, h) and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546.

In the present case the important factors leading to a conclusion of undue experimentation are the absence of any working example of a formed solvate, the lack of predictability in the art, and the broad scope of the claims.

g) The state of the art is that is not predictable whether solvates will form or what their composition will be. In the language of the physical chemist, a solvate of organic molecule is an interstitial solid solution. This phrase is defined in the second paragraph on page 358 of West (Solid State Chemistry). West, Anthony R., "Solid State Chemistry and its Applications, Wiley, New York, 1988, pages 358 & 365. The solvent molecule is a species introduced into the crystal and no part of the organic host molecule is left out or replaced. In the first paragraph on page 365, West (Solid State Chemistry) says, "it is not usually possible to predict whether solid solutions will form, or if they do form what is their compositional extent". Thus, in the absence of experimentation one cannot predict if a particular solvent will solvate any particular crystal. One cannot predict the stoichiometery of the formed solvate, i.e. if one, two, or a half a molecule of solvent added per molecule of host. In the same paragraph on page 365 West (Solid State Chemistry) explains that it is possible to make meta-stable non-equilibrium solvates, further clouding what Applicants mean by the word solvate. Compared with polymorphs, there is an additional degree of freedom to solvates, which means a different solvent or even the moisture of the air that might change the stabile region of the solvate.

h) The breadth of the claims includes all of the hundreds of thousands of compounds of formula I as well as the presently unknown list of solvents embraced by the term "solvate". Thus, the scope is broad.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear what does the term "medicament" mean. Is it a composition containing a therapeutically effective amount of a medicine? Or is it administration of a medicine to cause an effect in treating one of the disorders? The claims are considered hybrid claims containing multiple categories of invention i.e. both composition and method of use. The claims are confusing and indefinite as explained: If the claims are drawn to pharmaceutical composition, how many are there? Please note that treatment of disease or disorder in current practice is pathology or symptom oriented. The effective process/composition of regulation of appetite would require decrease/increase of food intake. Such a process/composition would be detrimental to the person who is anorexic or bulimic or obese. In addition, for a composition to be effective in treating diabetes, a process/effective amount of lowing blood glucose

(please note that treating diabetes or diabetic complication are different disorders) is needed; for treating cardiovascular disorder such as ischemic coronary disorder, an coronary vasodilating process/effective amount is needed; for treating epilepsy, an anticonvulsive process/effective amount is needed, etc. Therefore, it is unclear how many compositions or processes are encompassed by the claims. In addition, the claimed processes or compositions are intended for accomplishing opposite effects such as treating obesity and bulimia at the same time which is incredible. Furthermore, the claims also include "prophylaxis" which is self conflicting since for example if the composition is for "improvement" or "treatment" of a diagnosed disorder, there could not be any de novo prophylaxis efficacy.

The limitation “combination, characterized in that it comprises at least one…” in the Markush groups of claims 1-5 is indefinite. First, it is improper to use the open language “comprising” in a Markush group because the optional choices do not compose a closed set (see MPEP § 2173.05(h)). Further, this limitation is indefinite because it is unclear what is meant by a combination that comprises one of the elements from the list, which is a combination encompassed by the phrase “at least one”. What else are the elements combined with to form a combination comprising one of the elements? Thus, the metes and bounds of patent protection sought for the instantly claimed formulations have not been defined.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 4-5 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-5 provides for the use of the combination of a compound with NPY (neuropeptide Y) receptor affinity with at least one compound of 5-HT6 receptor affinity in the manufacture of a medicament for simultaneous neuropeptide Y5- and 5-HT6 receptor regulation and use of such combination for the manufacture of a medicament for regulation of appetite but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Please note that for examination purposes the claims 4 and 5 will be examined as method of regulation of appetite claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed to an active substance combination of at least one compound with neuropeptide receptor Y (NPY) affinity (formula I a) and at least one compound with 5-HT6 receptor affinity (formula I b) or medicament comprising the same or the use of the combination for the manufacture of a medicament for prophylaxis or treatment of various disorders including regulation of appetite, Azheimer's Parkinson's, arthritis, cachexia, bulmia, anorexia etc. The claims are very broad in scope with respect to the number of compounds in combination, in preparation of the medicament and use of such combination in manufacture of a medicament. The specification provides guidance to synthesis of the compounds that bind to NPY receptor and binding results for some of the representative compounds of formula (Ia-Ih) to NPY receptor and 5-HT6 receptor. A medicament is defined as 'An agent that promotes recovery from an injury or ailment; a medicine". The specification does not provide any guidance of making a medicament comprising at least one compound with neuropeptide receptor Y (NPY) affinity and at least one compound with 5-HT6 receptor affinity. The specification does not provide guidance to any steps involved in the method/process of making the medicaments. If a medicament is used in combination for therapy the formulations comprising the active agents can be used in

different formulations (e.g. for sequential administration) or in a single formulation. If the medicament with the active agents is in a single pharmaceutical formulation then a person of ordinary skill in the art has to do an undue experimentation to prepare such a combination with the active substances claimed as in combination therapy potential drug interactions, toxicity measurements etc need to be considered. Applicants' have claimed the same active substance combination as a medicament for treating various disorders such as bulimia and anorexia. It is not predictable from the guidance given by the Applicants' (synthesis of the compounds with NPY receptor affinity and binding affinity for some representative samples of the compounds synthesized) that the same medicament or composition is manufactured for treating obesity and bulimia. It is not predictable from the guidance given by the Applicants' that the same medicament or pharmaceutical formulation is manufactured for treating cardiovascular disorders and Alzheimer's. It is hard to predict whether the same medicament is used in treating various disorders claimed because each disease has a different and distinct etiology and pathophysiological manifestations, and that each is differently treated. Applicants' have not provided any guidance to making any of the pharmaceutical compositions with active substances in combination. It is not clear from the specification whether any amount of active substance that has neuropeptide receptor affinity (formula I a) in combination with any amount of a compound that has 5-HT6 receptor affinity (formula I b) will simultaneously regulate neuropeptide Y and 5-HT6 receptor. A skilled artisan would not recognize that Applicants' were in possession of the claimed invention, 'medicament comprising an active substance combination to any one of the claims 1-4

for simultaneous neuropeptide Y and 5-HT6 receptor regulation and the manufacture of such a medicament.

Claim Rejections - 35 USC § 103

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

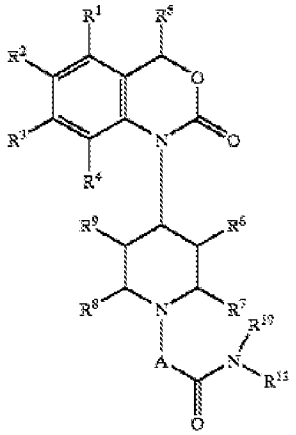
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 30-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jover et al. (US 2004/0058920, filing date Apr 4 2003) in view of Merce-Vidal et al. (U.S. 7,105,515, effective filing date Nov 13 2002) and Caldirola et al. (U.S. 7,144,883, effective filing date, June 11 2002).

Jover et al. teaches benzoxazinone- derived compounds of formula I as claimed in the instant application, their compositions and their use as a medicament in treatment of humans or animals (see abstract, para 0010). The reference teaches A can be CH2 (para 0015), R10 can H and R11 can be heteroaryl radical (para 0017), then it can read on the elected species.

(I)



The reference further teaches that the compositions comprising the compound can be formulated into orally administrable form containing one or more physiologically compatible carriers or excipients, and may take any convenient form, such as tablets, pellets, capsules, lozenges, aqueous or oily solutions, suspensions, emulsions, or dry powdered form suitable for reconstitution with water or other suitable liquid medium before use, for immediate or controlled release (para 0288). The reference teaches the compounds as neuropeptide Y receptor regulators are useful for the regulation of food ingestion (para 009) and in the treatment of treatment of disorders of food ingestion, preferably obesity, anorexia or bulimia (para 0285). In para 003, the reference teaches

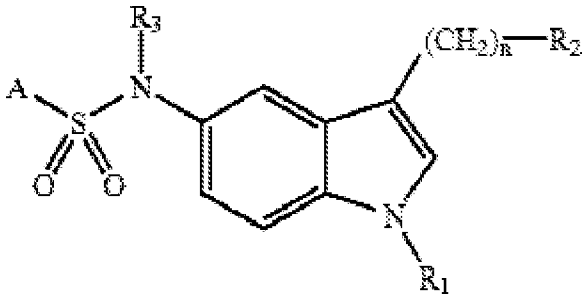
that NPY (neuropeptide Y) is a powerful stimulant of food ingestion and thus appetite is significantly increased when NPY is injected directly into the CNS of satiated mice.

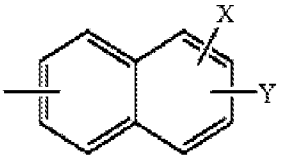
It would have been obvious to one having ordinary skill in the art at the time of the invention to have used compounds of formula I a in regulation of appetite because of the teachings of Jover et al. Jover et al. teaches that NPY (neuropeptide Y) is a powerful stimulant of food ingestion and thus appetite is significantly increased and further teaches that the compounds of formula I a can be used in regulation of food ingestion. Thus it would have been obvious to one having ordinary skill in the art to have used the claimed compounds in regulation of appetite because the compound are taught to be NPY regulators and NPY regulation regulates the appetite according to Jover et al. One having ordinary skill in the art would have been motivated to use the compounds in a method of regulation of appetite in order to treat the food ingestion disorders including obesity, bulimia etc.

The reference does not teach a 5-HT6 receptor affinity compound in the active substance combination.

The reference Merce-Vidal teaches derivatives of sulphonamides (see abstract).

(I)



When R1=H, n=0, A= 

, R3=H the reference teaches the elected species for 5-HT6 (see col. 2, lines 50, 65, 67, col. 3, line 24). The reference provides guidance towards the synthesis of the sulfonamide compounds, its pharmaceutical formulation the amount of daily doses (1-500 mg) in human medicine (see col. 33, lines 55-67, col. 34, example 1). Merce-Vidal teaches that the compounds have 5-HT6 serotonin receptor antagonistic activity useful in the preparation of medicament for prevention or treatment of various CNS (central nervous system) disorders.

Caldirola et al. teaches substituted sulfonamide compounds with 5-HT6 receptor affinity to be useful for the prophylaxis and treatment of medical conditions relating to obesity, type II diabetes and/or disorders of the central nervous system (see abstract, col. 2, lines 31-35). The reference teaches preparation of such compounds, pharmaceutical formulations and a method of using such compounds in treating obesity (col. 107, claims 7-9).

It would have been obvious to one having ordinary skill in the art at the time of the invention to have combined a compound of the instantly claimed with that of a compound with 5-HT6 serotonin receptor affinity from the teachings of Jover and Merce-Vidal. Jover teaches some of the instantly claimed compounds as NPY affinity compounds and can be used in treating CNS disorders. Merce-Vidal teaches 5-HT6 compounds as claimed including the elected species. Merce-Vidal and Caldirola et al.

teaches the use of 5-HT6 receptor binding compounds to be useful in obesity, CNS disorders. It would have been obvious to one having ordinary skill in the art at the time of the invention to have made a combination or a formulation or a medicament of at least one compound of the instantly claimed with at least one compound with 5-HT6 receptor affinity because both of them have been taught in the prior art to be useful in a method of treating CNS disorders. One having ordinary skill in the art would have been motivated in making such a medicament combination in expectation of using the same in a method of treating CNS disorders. One of ordinary skill in the art would have been motivated to incorporate the two agents herein in a single combination pharmaceutical composition because combining the agents herein each of which is known to be useful to treat depression individually into a single composition useful for the very same purpose is *prima facie* obvious. See *In re Kerkhoven* 205 USPQ 1069. It would have been obvious to one having ordinary skill in the art at the time of the invention to have manufactured the medicament combining NPY receptor affinity compound with 5HT-6 receptor affinity compound to use in regulation of appetite because the prior art shown above teaches the preparation of pharmaceutical formulations of the active medicaments and their use in treating obesity. Obesity is an eating disorder and a root cause for obesity is excessive consumption of food. Appetite is a desire to eat food when hungry and abnormal appetite could lead to an eating disorder, obesity. Hence treating obesity condition leads to suppression of appetite or regulation of appetite. It would have been obvious to one having ordinary skill in the art at the time of the invention to have made a medicament comprising an active substance combination of a

compound with neuropeptide receptor affinity with that of a compound with 5-HT6 serotonin receptor affinity or use of the combination for the manufacture of a medicament for simultaneous neuropeptide Y5 and 5-HT6 regulation. The references do not explicitly teach the amounts of NPY receptor affinity compound and 5-HT6 receptor affinity compound for active substance combination or in a medicament. However, the references in general teaches dosage amounts of NPY receptor affinity compound and 5-HT6 receptor affinity compounds in making formulations or medicaments and in the manufacture of the same. It would have been obvious to one of ordinary skill in the art at the time of the invention to have adjusted the amounts of component A and component B as claimed by the Applicants (claim 4) through routine experimental procedure. Generally, the ratios of concentration will not support the patentability unless there is evidence indicating such concentration is critical. "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,456, 105 USPQ 233, 235 (CCPA 1955).

Claims 34-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jover et al. (US 2004/0058920, filing date Apr 4 2003) in view of Merce-Vidal et al. (U.S. 7,105,515, effective filing date Nov 13 2002) and Caldirola et al. (U.S. 7,144,883, effective filing date, June 11 2002) as applied to claims 1-5, 30-33 above and further in view of Noda et al. (U.S. 5,320,853).

Jover, Merce-Vidal et al. and Caldirola et al teachings discussed as above.

The references do not teach the pharmaceutical formulation in a sustained release form.

Noda et al. teaches controlled release formulation for pharmaceutical compounds. The reference teaches a coat and sustainable drug releasing exterior coat (see Abstract). The reference teaches water insoluble polymers including ethylcellulose, cellulose acetate (col.2, lines 40-45), drug releasing polymers such as acrylates and/or methacrylates (Eudagrit) (col. 5, lines 10-20, col. 6, lines 55-65), plasticizers (col. 5, lines 37-40) and white wax (also known as beeswax) (col. 9, line 8) in the sustained release formulation.

It would have been obvious to one having ordinary skill in the art at the time of the invention to have made a controlled release drug delivery device with combination of a compound of the instantly claimed with that of a compound with 5-HT6 serotonin receptor affinity because it within the knowledge of the skilled pharmacologist to make differential release composition as they represent conventional formulations and modes of administration. It is well known from the prior art teachings like Noda et al. that such conventional formulations can be made. One having ordinary skill in the art at the time of the invention would have been motivated to make a controlled release formulation of the active substance combination claimed in order for once or twice a day administration of the drugs and achieve desired blood levels of the drugs in a manner which delays or sustains the release of the drug. It would have been obvious to one having ordinary skill in the art to formulate a composition where one of the components (A) or (B) as claimed is in a non-sustained release dosage form is in case of a medical

condition where one of the components needs to be delivered without any controlled drug delivery.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to UMAMAHESWARI RAMACHANDRAN whose telephone number is (571)272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shengjun Wang/

Primary Examiner, Art Unit 1627